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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 4

Complete if Known

Application Number 09/986,426
Filing Date November 8, 2001
First Named Inventor Randal J. KIRK, et al
Group Art Unit 1651
Examiner Name To Be Assigned
Attorney Docket Number 54719.000011

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
DFW	U1	3,846,399		Hirschmann et al.	11/05/74	
DFW	U2	4,040,907		Ullman et al.	08/09/77	
DFW	U3	4,356,166		Peterson et al.	10/26/82	
DFW	U4	4,399,121		Albarella et al.	08/16/83	
DFW	U5	4,552,864		Antoni et al.	11/12/85	
DFW	U6	4,863,735		Kohn et al.	09/05/89	
DFW	U7	4,976,962		Bichon et al.	12/11/90	
DFW	U8	5,087,616		Myers et al.	02/11/92	
DFW	U9	5,238,714		Wallace et al.	08/24/93	
DFW	U10	5,534,496		Lee et al.	07/09/96	
DFW	U11	5,762,909		Uzgiris	06/09/98	
DFW	U12	5,767,227		Latham et al.	06/16/98	
DFW	U13	5,846,743		Janmey et al.	12/08/98	
DFW	U14	5,851,536		Yager et al.	12/22/98	
DFW	U15	5,882,645		Toth et al.	03/16/99	
DFW	U16	5,910,569		Latham et al.	06/08/99	
DFW	U17	5,948,750		Garsky et al.	09/07/99	
DFW	U18	5,952,294		Lazo et al.	09/14/99	
DFW	U19	5,977,163		Li et al.	11/02/99	
DFW	U20	6,030,941		Summerton et al.	02/29/00	
DFW	U21	6,306,993	B1	Rothbard et al.	10/23/01	
DFW	U22	5,073,641		Bundgaard et al.	12/17/91	

FOREIGN PATENT DOCUMENTS

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		Office ³	Number ⁴	Kind Code ⁵ (if known)				
DFW	F1	WO	97/36616		Seymour et al.	10/09/97		

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Sheet 2 of 4

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First Named Inventor	Randal J. KIRK et al.
Group Art Unit	1651
Examiner Name	To Be Assigned
Attorney Docket Number	54719.000011

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
DFW	P1	ORTEN, James M. et al., "Thyroxine," <i>Human Biochemistry</i> , 9 th Ed., C.V. Mosby Company, St. Louis, pp. 401-405 (1975).	
DFW	P2	LI, Chun, et al., "Complete Regression of Well-Established Tumors Using a Novel Water-Soluble Poly(L-Glutamic Acid)-Paclitaxel Conjugate," <i>Cancer Res</i> , 58:2404-2409 (1998).	
DFW	P3	KRAMER, Werner et al., "Intestinal Absorption of Peptides by Coupling to Bile Acids," <i>The Journal of Biochemistry</i> , 269(14):10621-10627 (1994).	
DFW	P4	RAWITCH, Allen B., et al., "The Isolation of Identical Thyroxine Containing Amino Acid Sequences from Bovine, Ovine and Porcine Thyroglobulins," <i>Biochemical and Biophysical Research Communications</i> , 118(2):423-429 (1984).	
DFW	P5	MARRIO, Claudine, et al., "Amino Acid Sequence of the Unique 3,5,3'-Triiodothyronine-Containing Sequence from Porcine Thyroglobulin," <i>Biochemical and Biophysical Research Communications</i> , 112(1):206-213 (1983).	
DFW	P6	SAWADA, Kyoko, et al., "Recognition of L-Amino Acid Ester Compounds by Rat Peptide Transporters PEPT1 and PEPT2," <i>Journal of Pharmacology and Experimental Therapeutics</i> , 291(2):705-709 (1999).	
DFW	P7	DE VRUEH, Remco L.A., et al., "Transport of L-Valine-Acyclovir Via the Oligopeptide Transporter in the Human Intestinal Cell Line, Caco-2," <i>Journal of Pharmacology and Experimental Therapeutics</i> , 286(2):1166-1170 (1988).	
DFW	P8	GUO, Ailan, et al., "Interactions of a Nonpeptidic Drug, Valacyclovir, with the Human Intestinal Peptide Transporter (hPEPT1) Expressed in a Mammalian Cell Line," <i>Journal of Pharmacology and Experimental Therapeutics</i> , 289(1):448-454 (1999).	
DFW	P9	BURNETTE, Thimysta C., et al., "Metabolic Disposition of the Acyclovir Prodrug Valacyclovir in the Rat," <i>Drug Metabolism and Disposition</i> , 22(1):60-64 (1994).	
DFW	P10	AGGARWAL, et al., "Synthesis and Biological Evaluation of Prodrugs of Zidovudine," <i>J. Med. Chem.</i> , 33(5):1505-1511 (1990).	
DFW	P11	ZUNINO, Franco, et al., "Comparison of Antitumor Effects of Daunorubicin Covalently Linked to Poly-L-Amino Acid Carriers," <i>European Journal of Cancer & Clinical Oncology</i> , 20(3):121-125 (1984).	
DFW	P12	HAVRANOVA, Marie et al., "A High-Molecular Mass Derivative of Trypsin-Kallikrein Inhibitor for Potential Medical Use, II," <i>Hoppe-Seyler's Z. Physiol. Chem.</i> , 363:295-303 (1982).	
DFW	P13	RYSER, Hugues J.P., et al., "Conjugation of Methotrexate to Poly (L-lysine) Increases Drug Transport and Overcomes Drug Resistance in Cultured Cells," <i>Proc. Natl. Acad. Sci. USA</i> , 75(8):3867-3870 (1978).	
DFW	P14	HAN, Hyo-Kyung, et al., "Targeted Prodrug Design to Optimize Drug Delivery," <i>AAPS PharmSci</i> , 2(1): Article 6 (2000).	
DFW	P15	TAMAI, I., et al., "Improvement of L-dopa Absorption by Dipeptidyl Derivation, Utilizing Peptide Transporter PepT1," <i>J. Pharma. Sci.</i> , 87(12):1542-1546 (1988), Abstract.	

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Sheet 3 of 4

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Group Art Unit	1651
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OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

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DFW	P16	OH, D.M., et al., "Drug Transport and Targeting. Intestinal Transport," <i>Pharma Biotechnol.</i> , 12:59-88 (1999), Abstract.	
DFW	P17	BALIMANE, P., et al., "Effect of Ionization on the Variable Uptake of Valacyclovir via the Human Intestinal Peptide Transporter (hPEPT1) in CHP cells," <i>Biopharm Drug Dispos.</i> , 21(5):165-174 (2000), Abstract.	
DFW	P18	KNUTTER, I, et al., "A Novel Inhibitor of the Mammalian Peptide Transporter PEPT1," <i>Biochemistry</i> , 40(14):4454-4458 (2001), Abstract.	
DFW	P19	SHEN, H., et al., "Developmental Expression of PEPT1 and PEPT2 in Rat Small Intestine, Colon, and Kidney," <i>Pediatr Res</i> , 49(6):789-795 (2001), Abstract	
DFW	P20	FRIEDRICHSEN, G.M., et al., "Model Prodrugs Designed for the Intestinal Peptide Transporter. A Synthetic Approach for Coupling of Hydroxy-Containing Compounds to Dipeptides," <i>Eur J Pharm Sci</i> , 14(1):13-19 (2001), Abstract.	
DFW	P21	HAN H., et al., "5'-Amino Acid Esters of Antiviral Nucleosides, Acyclovir, and AZT and Absorbed by the Intestinal PEPT1 Peptide Transporter," <i>Pharm Res</i> , 15(8):1154-1159 (1998), Abstract.	
DFW	P22	BLIMANE, P.V., et al., "Direct Evidence for Peptide Transporter (PepT1)-Mediated Uptake of a Nonpeptide Prodrug, Valacyclovir," <i>Biochem Biophys Res Commun</i> , 250(2):246-251 (1998), Abstract.	
DFW	P23	HAN, H.K., et al., "Cellular Uptake Mechanism of Amino Acid Ester prodrugs in Caco-2hPEPT1 Cells Overexpressing a Human Peptide Transporter," <i>Pharm Res</i> , 15(9):1382-1386 (1998), Abstract.	
DFW	P24	SHIRAGA, T., et al., "Cellular and Molecular Mechanisms of Dietary Regulation on Rat Intestinal H+/Peptide Transporter PepT1," <i>Gastroenterology</i> , 116(2):354-362 (1999), Abstract.	
DFW	P25	GUO, A., et al., "Interactions of a Nonpeptidic Drug, Valacyclovir, with the Human Intestinal Peptide Transporter (hPEPT1) Expressed in a Mammalian Cell Line," <i>Pharmacol Exp Ther</i> , 289(1):448-454 (1999), Abstract.	
DFW	P26	AMIDON, G.L., et al., "5'-Amino Acid Esters of Antiviral Nucleosides, Acyclovir, and AZT are Absorbed by the Intestinal PEPT1 Peptide Transporter," <i>Pharm Res</i> , 16(2):175 (1999), Abstract.	
DFW	P27	LEIBACH, F.H, et al., "Peptide Transporters in the Intestine and the Kidney," <i>Annu Rev Nutri</i> , 16:99-119 (1996), Abstract.	
DFW	P28	HERRERA-RUIZ, D., et al., "Spatial Expression Patterns of Peptide Transporters in the Human and Rat Gastrointestinal Tracts, Caco-2 in vitro Cell Culture Model, and Multiple Human Tissues," <i>AAPS PharmSci</i> , 3(1):E9 (2001), Abstract.	
DFW	P29	TOTH, Istvan, "A Novel Chemical Approach to Drug Delivery: Lipidic Amino Acid Conjugates," <i>Journal of Drug Targeting</i> , 2:217-239 (1994).	
DFW	P30	NEGISHI, Naoki, et al., "Coupling of Naltrexone to Biodegradable Poly (α -Amino Acids)," <i>Pharmaceutical Research</i> , 4(4):305-310 (1987).	

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Deborah K. Wang

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Sheet	14	of	4
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